In Vivo Characterization of White Matter Microvasculature Anisotropy with Diffusion-Weighted MRI

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Introduction:
Disorders of the cererbral microvasculature and blood perfusion anomalies involve virtually every disease process in the human brain (e.g. strokes, tumor, and trauma). Since there are cellular and functional interactions between capillaries, glia and neurons ("neurovascular unit"), local perfusion is inextricably coupled to the health of the central nervous system. Moreover, there are eloquent areas of the parenchyma where the microvascular architecture is not random but it conforms to the white matter tracts [1], so characterizing the microcirculation there could provide an adjunctive diagnostic tool. In all commonly used cerebral perfusion methods (Dynamic Susceptibility Contrast- DSC and Arterial Spin Labeling- ASL), which employ the central volume theorem, the microvascular network is assumed to be isotropic. To our knowledge only Thacker [2] proposed a directional flow model as an alternative approach for Cerebral Blood Flow (CBF) calculation from DSC measurements. In this study, we employ low b-value Diffusion Weighted Imaging, an inherently directional sensitive method, to produce measures of microvasculature anisotropy in a few brain territories, and then correlate these measures with DTI fractional anisotropy measurements.

Materials and Methods:

Theory: We consider that the microvasculature consists of two compartments corresponding to different levels of blood flow velocities: higher velocities occur in vessels and larger microvessels (arterioles and venules) and lower velocities occur in smaller microvessels (capillaries). Extending the IntraVoxel Incoherent Motion technique (IVIM) [3], we propose a three-compartment model for the MR diffusion signal, representing intravascular fast flowing spins (apparent volume fraction f_f), intravascular slow flowing spins (apparent volume fraction f_s) and spins diffusing in extravascular space (apparent volume fraction 1- f_f -f_s). If F_f and F_s are the fast and

$$\frac{S(b)}{S_0} = f_f F_f(b)\exp(-bD_{in}) + f_s F_s(b)\exp(-bD_{in}) + (1 - f_f - f_s)\exp(-bD_{ex}) \quad (1)$$

$$\frac{S(b_1)}{S_0} = f_s F_s(b_1)\exp(-bD_{in}) + (1 - f_f - f_s)\exp(-b_1 D_{ex}) \cong 1 - f_f \quad (2)$$

$$\frac{S(b)}{S_0} = (1 - f_f - f_s)\exp(-bD_{ex}) \quad (3)$$

slow microflow attenuation factors and D_{in} and D_{ex} the diffusion coefficients in intravascular and extravascular space, then the signal attenuation can be described by Eq. (1). For a low b-value (b_1 of the order of 10-15 s/mm^2), which for a typical IVIM acquisition corresponds to a velocity cut-off 4-5 mm/s, an estimate of the apparent fast vascular volume fraction can be obtained (Eq. 2). The perfusion signal is nearly completely attenuated for b>200 s/mm^2, and Eq. (3) can provide an estimate for the total vascular volume fraction. We also apply the above model for every diffusion gradient direction independently.

Data acquisition: A series of diffusion weighted images is obtained on a human volunteer with a stimulated-echo diffusion-weighted sequence with interleaved variable density spiral encoding on a head-only Siemens Allegra 3T system. A 16-shots acquisition strategy with an oversampling factor of 4 is followed. The imaging parameters are: FOV=24 cm, slice thickness=8 mm, acquisition matrix=128x128, TR/TE=1200/50 ms, N_{ex}=1. Peripheral gating is used with a trigger delay of 50 ms to reduce the sensitivity of the acquisition to pulsatile blood flow. 15 b-values are used along the three logical axes of the acquisition (X, Y, Z, as shown in Fig. 1a) with diffusion encoding parameters: δ=16 ms, Δ=50 ms and g_{max}=28 mT/m, corresponding to b_{max}=660 s/mm^2. Motion correction is performed separately for each interleaf using the center k-space data according to the imaging space phase-correction algorithm described by Liu [4]. The total scan time is 24 minutes.

Results:
Two ROIs are highlighted in Fig. 1a located on the corticospinal tracts (3x4 pixels-ROI A) and also on a portion the corpus callosum (2x7 pixels-ROI B). The echo attenuation variation in the midbrain ROI for the full range of b-values and for the low b-value regime is plotted in Figs. 1c and 1d. The results for f_f, derived from Eq. (2), and $f_{tot}= f_f+ f_s$, derived from the asymptotic fit of Eq. (2) are given in Table 1. IVIM clearly reveals a preferential orientation of the apparent vascular volume fraction that coincides with the tracts orientation for the cortico-spinal tract ROI (Fig. 1b). The apparent vascular volume fraction values can be converted to Cerebral Blood Volume (CBV) values using the relationship CBV=100 f_s f_w/ρ where f_w is the MR-visible water content of tissue [5]. Based on of Neeb [6], we use f_w=0.70 for white matter and the results of a direction sensitive CBV are summarized in Table 1. The IVIM results for the corpus callosum ROI show a left-right preferential orientation, and thus are also consistent with the DTI results.

Discussion:
IVIM technique suffers from the known limitations of high SNR requirement, susceptibility artifacts and the difficulty in the interpretation of the derived parameters. In the current study, we address the first two limitations by implementing a multi-shot self-navigating DW imaging technique. Furthermore, we are focusing only on the extracted vascular volume fraction, avoiding the ambiguity that exists for the pseudo-diffusion coefficient [6]. The asymptotic model fit is based on the high b-value regime and is less sensitive to noise contamination [5]. The derived CBV values show a clear directional dependence and the mean CBV value averaged over the 3 applied diffusion directions is equal to 3 ml/ 100g and therefore comparable to the CBV values measured with ASL and DSC in white matter.
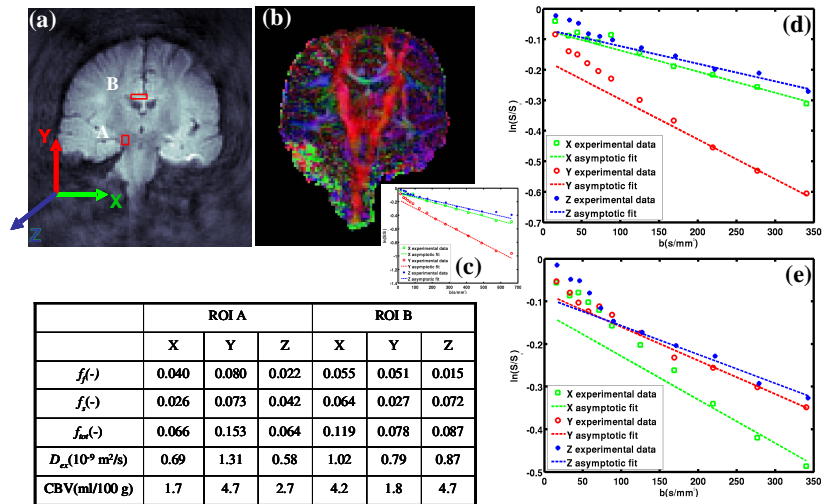

Figure 1: (a) ROI positions on a DW image of a coronal slice: 3x4 ROI (A) in corticospinal tracts and 2x7 ROI (B) in corpus callosum, (b) color coded FA map showing main tracts orientation, (c) full plot of the normalized diffusion signal as a function of diffusion weighting b for 3 directions for ROI A in log-linear scale, (d-e) plots of the normalized diffusion signal as a function of diffusion weighting b for b<200 s/mm^2 for 3 directions for ROI A (d) and ROI B (e) in log-linear scale.

Table 1: Summary of model fit parameters for the two given ROIs.

	ROI A			ROI B		
	X	Y	Z	X	Y	Z
f_f(-)	0.040	0.080	0.022	0.055	0.051	0.015
f_s(-)	0.026	0.073	0.042	0.064	0.027	0.072
f_{tot}(-)	0.066	0.153	0.064	0.119	0.078	0.087
D_{ex}(10^{-9} m^2/s)	0.69	1.31	0.58	1.02	0.79	0.87
CBV(ml/100 g)	1.7	4.7	2.7	4.2	1.8	4.7

Conclusion: We demonstrate that the current implementation of the IVIM technique can provide direction-sensitive estimates of CBV which are consistent with the expected local orientation of microvessels and can thus probe the microvasculature in selected territories of the brain parenchyma.

References:
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